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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,339	01/28/2002	Saverio Carl Falco	BB1067 US CNT	4340

23906 7590 04/20/2004

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LEGAL PATENT RECORDS CENTER
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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,339	FALCO ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/22/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 14-33* is/are pending in the application.

4a) Of the above claim(s) *26-28 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,14-25,29 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/20/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Applicant's election without traverse of Group I (Claims 14-25, 29 and 31-33) in the response filed 9/29/03 is acknowledged.

Claims 26-28, 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 9/29/03.

It is noted that the examiner, in the restriction requirement mailed 8/26/03, neglected to include pending Claim 1 in Group I. Claim 1 will be examined along with elected Group I.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Specifically, hyperlinks are present on pages 8, 9 and 29 of the specification. Applicants are encouraged to review to the specification and delete any other embedded hyperlinks and/or other forms of browser-executable code.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14-25, 29, 31-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to claim 1, applicants recite an isolated nucleic acid fragment which comprises a partial cDNA sequence (SEQ ID NO:s 7 and 9) for a wheat methionine synthase (MS) or the complement thereof or degenerate sequence in accordance with the degeneracy of the genetic code. There is actual reduction to practice of the disclosed species. The claim therefore reads on a genus of sequences which minimally contain SEQ ID NO:7 and/or 9 and wherein said genus of sequences includes any full length gene which contains the sequences, any fusion constructs or cDNAs, etc.

With regard to claims 14-15, 18-25, 29 and 31-33, applicants recite a genus of nucleic acid sequences encoding SEQ ID NO:s 2 and 4 (or complements thereof) and sequences having at least 90% sequence identity based upon the Clustal alignment method, as well as vectors, cells and plants containing said sequences and methods of using said sequences to increase methionine content of plants or making methionine in cells *in vitro*. There is actual reduction to practice of the disclosed species SEQ ID NO:2 and 4.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show that applicant was in possession of the claimed invention. In the case of claim 1, a partial cDNA sequence that is claimed with open language (comprising) encompasses a variety of subgenera with varying characteristics. For example, a cDNA's principle attribute would include its coding region. A partial cDNA that did not include a disclosure of any open reading frame of which it would be a part, would not be representative of the genus of cDNAs because no information regarding the coding capacity of any cDNA molecule would be disclosed. Further, defining the cDNA in functional terms would not suffice in the absence of a disclosure of structural features or elements of a cDNA that would encode a protein having a stated function. The instant specification discloses a single common structural feature shared by the members of the claimed genus, i.e. SEQ ID NO:7 and/or 9. Since the claimed genus encompasses cDNAs and genes yet to be discovered, DNA constructs that encode fusion proteins, etc., the disclosed structural feature does not constitute a substantial portion of the claimed genus. Therefore the disclosure of SEQ ID NO:s 7 and 9 does not provide an adequate description of the claimed genus.

With regard to claims 14-15, 18-25, 29 and 31-33, applicants claim the recited nucleic acid sequences by functional characteristics without presenting any functional motifs which characterize the biological activities of MS genes. Without a correlation between structure and function or an identification of relevant identifying characteristics conserved in MS genes, it is unclear how the skilled artisan would identify additional members of the claimed genus. The general knowledge in the art concerning MS genes does not provide any indication of how the structure of one MS gene is

representative of unknown MS genes. The common attributes of the claimed genus are not described. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of the disclosed members of the genus is not representative of the genus claimed.

Finally, the nucleic acid sequences recited in claims 1, 14-25, 29 and 31-33 read on cDNAs or portions of cDNAs encoding MS polypeptides; however, use of the open transitional phrase "comprising" with regard to the recited nucleotide sequences renders all of the claims readable on the genomic versions of the claimed sequences. Applicants have not disclosed the genomic versions of any of the recited sequences and the 5' and 3' regulatory regions, introns, etc. cannot be described given the cDNA sequence or portions of cDNA sequences. The regulatory regions, introns, etc. must be determined empirically.

Claims 14-25, 29 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleotide sequences (SEQ ID NO:s 1 and 3) encoding SEQ ID NO:s 2 and 4, vectors and cells and plants containing said sequences and methods of producing methionine and methods of increasing the methionine content of seeds, said methods using SEQ ID NO:s 1 and 3, does not reasonably provide enablement for nucleotide sequences encoding methionine synthase proteins having at least 90% sequence identity with SEQ ID NO:s 2 and 4 using the Clustal alignment method. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants claim isolated nucleic acid sequences encoding plant MS proteins, wherein said proteins are SEQ ID NO:2 and 4 and sequences at least 90% identical thereto based upon the Clustal alignment method. Applicants also claim vectors, cells and plants containing said sequences as well as methods of making methionine and increasing the methionine content of plants using said nucleic acid sequences.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reaches by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following: 1) Unpredictability of the art. The art with regard to isolation of unknown genes encoding MS which are at least 90% identical to SEQ ID NO:2 and 4 based upon the Clustal method must be considered unpredictable. It is noted that the prior art (Eichel et al., Eur. J. Biochem., 1995, Vol. 230, pp. 1053-1058, cited by applicants) indicates that "Methionine synthase enzymes from plants are not well characterized..." (p. 1053, right column). Given that neither applicants nor the art provides a disclosure concerning the functional motifs of the MS, the skilled artisan would need to essentially practice trial and error experimentation to attempt to make sequences encoding MS and test said

sequences to ascertain if they had MS activity. While it can be argued that the skilled artisan could assay the expression product of any given nucleic acid sequence for MS activity, this would involve a method for **identifying** sequences within the confines of the claimed subject matter, not a method of **making** said sequences.

2) State of the art. The state of the art is poorly developed. As noted above plant MS genes, at the time of applicants invention, were poorly characterized.

3) Number of working examples. Applicants present working examples for the MS cDNAs of tobacco, soybean, corn and partial sequences for wheat.

4) Amount of guidance provided by applicants. Applicants provide no guidance on how the skilled artisan would make sequences encoding biologically active MS polypeptides which have at least 90% amino acid identity to SEQ ID NO:2 or 4 based on the Clustal alignment method. While alignment of the sequences of the instantly disclosed amino acid sequences with each other and with the *C. roseus* MS sequence reveals considerable regions of homology, it is also noted that considerable variability exists between the different sequences and it is further noted that applicants have not even demonstrated that the instantly recited sequences have any MS activity.

5) Scope of the invention. The scope of the invention is broad. The claims read on potentially millions of different nucleic acid sequences which encode polypeptides which are at least 90% identical to SEQ ID NO:s 2 and 4 and have MS activity.

6) Nature of the invention. The invention involves the generation of nucleic acid sequences encoding polypeptides with MS activity and having at least 90% identity with SEQ ID NO:s 2 or 4.

7) Level of skill in the art. The level of skill in the art is high; however, given the unpredictability of the art, the poorly developed state of the art, the broad scope of the invention and the lack of guidance presented by applicants, the skilled artisan would have needed to essentially practice trial and error experimentation in order to attempt to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-25, 29 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-25, 29 and 31-33 are vague in that they recite sequences having at least 90% (or 95%) sequence identity to SEQ ID NO:2 or 4 based upon the Clustal alignment method. Without a recitation of the parameters used in the Clustal alignment, the metes and bounds of what sequences are included in the claims and what sequences are excluded are unclear.

Claim 25 is vague in the recitation of the phrase "...first nucleotide sequence is comprised by another polynucleotide..." because it is unclear whether the first

nucleotide sequence is a part of a larger second sequence or the second sequence is part of the first sequence. It is unclear if the 30 or more nucleotides of the first sequence are encompassed within the second sequence which encodes the polypeptide having MS activity or are separate from the second sequence?

Claims 31-32 are vague in that there is no antecedent basis for the term "...the **untransformed** (emphasis added) plant cells obtained from step (a)...".

Claim 33 is vague in that there is no antecedent basis for the term "...the chimeric gene..." in claim 19.

The closest prior art is exemplified by Eichel et al. (cited above). Eichel et al. teaches the gene (and deduced amino acid sequence) encoding the *C. roseus* MS protein but does not teach a nucleic acid sequence within the confines of the claimed invention.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
April 18, 2004

DAVID GUZO
PRIMARY EXAMINER